REMARKS

Entry of the foregoing, and early and favorable consideration of the subject application are respectfully requested.

By the present Amendment, the specification, in the Brief Description of the Drawings, has been amended to refer specifically to Figures 11A-11F, as requested by the Examiner at page 7 of the Official Action. Claims 129, 135, and 143-145 have been canceled without prejudice to or disclaimer of the subject matter contained therein. No new matter has been added.

Substance of Interview

Applicants gratefully acknowledge the courtesy shown to them, and to their representatives, by Examiner Marschel and Interference Practice Specialist Tsang in the personal interview held on August 13, 2003. In that interview, the outstanding rejections of the claims were discussed, as were possible arguments to overcome those rejections. Also discussed was Applicants' planned Request for Interference with U.S. Patent 6,025,126 to Westbrook. The Examiner indicated that he was inclined to recommend that an interference with the Westbrook patent should be declared upon resolution of the rejections of the claims.

INT. SUM. OK AM, 9-12-03

Claim Rejections – 35 USC 112, ¶ 2

Claims 127-149 are rejected under 35 USC 112, ¶ 2, as purportedly indefinite. At p. 3 of the official action, the Examiner suggests that the use of the acronyms "ABL" and "BCR" render the instant claims indefinite. This rejection is respectfully traversed.

Applicants respectfully maintain that one of ordinary skill in the art would readily understand these abbreviations, which are in common use in the art in connection with diagnosis of chronic myelogenous leukemia ("CML"). The Information Disclosure Statement, filed in this case on August 26, 2003, cites numerous scientific publications from the 1980s

relating to CML. These publications clearly show that the abbreviations "BCR" and "ABL" were in common use among those skilled in the art to refer to the genes containing the chromosomal breakpoints associated with CML and ALL. Applicants note that many of these publications are cited in the present specification, and are incorporated by reference (see ¶¶ 29-69). In view of the fact that these terms were well known in the art, they cannot render the present claims indefinite. Withdrawal of this rejection is thus respectfully requested.

Claim Rejections – 35 USC 112, ¶ 1 (Enablement)

Claims 127-136, 139-145, 148, and 149 are rejected under 35 USC 112, ¶ 1 as purportedly broader in scope than the enabling disclosure provided by the specification. This rejection is respectfully traversed.

At page 4 of the Official Action, the Examiner concedes that the present specification is "enabling . . . for chromosomal aberration locations in the BCR and ABL genes in the t(9;22)(q11:q34) site as claimed in claim 137." However, the Examiner argues that the present specification "does not reasonably provide enablement for any generic BCR/ABL gene aberrations." The basis for the Examiner's argument is set forth at page 5 of the Official Action.

> The usage for the instant invention is apparently directed to CML detection. The detection of a genetic aberration which is associated and diagnostic for a genetic disease is well known in the art to be a lengthy and unpredictable research process. Thus, without specific guidance regarding where an aberration occurs, it is unpredictable as to what other sites may or may not be for CML detection usage. Thus, the above listed claims contain a scope which goes beyond the specific breakpoint region which has been defined for CML detection practice which would require unpredictable and thus undue experimentation to determine other diagnostic sites by which to make and use hybridization probes for CML detection and/or diagnosis.

Applicants respectfully disagree.

The present claims are not specifically limited to CML detection, although that is one use for the probe sets of the present claims. The present claims are directed to probe sets for detecting chromosomal aberrations associated with the BCR and ABL genes. These probe sets

are useful, not only to diagnose CML, but also permit the user to distinguish between CML and acute lymphocytic leukemia (ALL), both of which result from chromosomal aberrations associated with the BCR and ABL genes (see, e.g., paragraphs 68, 79, and 168-172 of the instant application).

Applicants do not dispute that the initial detection of a genetic aberration that is associated with and diagnostic for a genetic disease can be a lengthy and unpredictable research process. However, the present claims are not directed to the initial detection of a genetic aberration that is associated with any particular disease; instead, they are related to probe sets associated with particular genes: the BCR and ABL genes. The chromosomal location and structure of the BCR and ABL genes was known in the art at the time the present application was filed, as was the involvement of translocations between these genes in particular diseases. For example, at p. 17, Applicants teach that

> Fusion of the proto-oncogene c-ABL from the long arm of chromosome 9 with the BCR gene of chromosome 22 is a consistent finding in CML (1-3). That genetic change leads to formation of a BCR-ABL transcript that is translated to form a 210 kd protein present in virtually all cases of CML (4-6). In 90% of the cases, the fusion gene results from a reciprocal translocation involving chromosomes 9 and 22 producing a cytogenetically distinct small acrocentric chromosome called the Philadelphia (Ph1) chromosome (7-12), Fig. 8.

The present claims recite that the claimed composition comprises two probes for detection of a chromosomal aberration: one that hybridizes to the ABL gene side of said chromosomal aberration, and another that hybridizes to the BCR gene side of said chromosomal aberration. As can be seen from the publications cited by Applicants in their recent IDS, the BCR and ABL genes were known to be present in publicly available cosmid libraries at the time the present application was filed. Armed with that knowledge, and the disclosure of the present application, one of ordinary skill in the art would have been able, at the time the present application was filed, to prepare probes that hybridize to the ABL and BCR genes in order to practice the presently claimed invention, using only routine experimental techniques. As discussed in the interview, knowledge of the complete sequence of the BCR and ABL genes was, and is, not

necessary for one of ordinary skill in the art to practice the claimed invention without the need for undue experimentation. The present application thus provides specific guidance regarding where chromosomal aberrations occur – in the BCR and ABL genes. The present claims provide probe sets that are directed to aberrations in those genes, the structures of which were known at the time the present application was filed. In summary, at the time the present application was filed, the structure of the BCR and ABL genes was known, material from which suitable probes could be made was available, and isolating such probes, even without knowledge of the detailed sequence of the BCR and ABL genes, would not require undue experimentation. Consequently, Applicants submit that the present claims clearly comply with the enablement requirement of 35 USC 112, ¶1. Withdrawal of the present rejection is thus respectfully requested.

Claim Rejections – 35 USC 112, ¶ 1 (Written Description)

Claims 127-149 are rejected under 35 USC 112, ¶ 1 as purportedly failing to comply with the written description requirement. This rejection is respectfully traversed.

The basis for this rejection is set forth at pp 5-6 of the Official Action, where the Examiner states that:

> The specification discloses ABL and BCR genes by name, but without any sequence information by which to design probes as instantly claimed which thus lack written description under the enablement provisions of 35 USC §112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claims. . . . .It is also noted that the sequences for the ABL and BCR genes are reasonably deemed essential subject matter for probe design.

Applicants respectfully disagree.

As discussed in the personal interview held on August 13, 2003, the present invention was made without knowledge of the complete sequence of the BCR or ABL genes. Instead, the present inventors used probes that had been constructed from libraries known to contain the

BCR and ABL genes. As noted above, useful libraries, and probes from such libraries, were available to those in the art at the time the present application was filed (and are still available). Thus, the complete sequences of the BCR and ABL genes are not essential subject matter to the present claims.

The test for compliance with the written description requirement is often phrased in terms of "possession:" does the specification convey with reasonable clarity to those skilled in the art that, as of the filing date sought, the applicants were in possession of the claimed invention. *See, e.g., Vas-Cath, Inc. v. Mahurkar,* 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). In view of the state of the art at the time the present application was filed, and the availability of materials from which useful probes could be constructed, one of ordinary skill in the art would not doubt that Applicants were in possession of the presently claimed invention at the time the application was filed, despite the fact that the complete sequence of the BCR and ABL genes is not provided in the specification. Consequently, the present application clearly complies with the written description requirement of 35 USC 112, ¶1. Withdrawal of this rejection is thus respectfully requested.

CONCLUSION

From the foregoing, Applicants submit that the present claims are in condition for allowance, and respectfully request an indication from the Examiner to that effect.

REQUEST FOR INTERFERENCE

Applicants respectfully request that an interference be declared between the application identified in caption and U.S. Patent No. 6,025,126[1] ("the '126 patent"). Applicants respectfully point out that examination of the present application should "be conducted with special dispatch" because it requests an interference with an issued patent. 37 CFR 1.607(b); MPEP 708.01 and 2307.

As explained in detail below, Applicants request that the interference be declared:

(i) employing the proposed Count set forth in attached Appendix A;

(ii) with claims 1-25 of the '126 patent and Claims 127-128, 130-134, 136-142, and 146-149 of the present application designated as corresponding to the Proposed Count; and

(iii) with Applicants indicated as being entitled to the benefit of application Serial No. 07/537,305 filed June 12, 1990[2].

Further, upon a determination by the Examiner that an interference should be recommended, immediate issuance of a Notice suspending prosecution pending declaration of an interference is respectfully requested.

In support of the Request for Interference, Applicants present below sections (1)-(6) corresponding to the pertinent sections of 37 CFR 1.607.

(1) Identifying the patent

The patent against which Applicants request an interference is U.S. Patent No.

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[1] Copies of the '126 patent and the other documents referred to herein are being concurrently submitted.

[2] The present application is a divisional of application Serial No. 08/487,974, filed June 7, 1995, which is a continuation of 08/342,028, filed November 16, 1994 (now abandoned), which is a continuation of application Serial No. 08/181,367, filed January 14, 1994 (now abandoned), which is a continuation of application Serial No. 08/054,353, filed April 28, 1993 (abandoned), which is a continuation of application Serial No. 07/537,305, filed June 12, 1990. While the application previously claimed the benefit of earlier applications, the priority claim has been amended to reflect the proper priority claim for the claims pending in the present application.

6,025,126 which lists as inventor Carol A. Westbrook. The patent issued February 15, 2000, and is assigned on its face to Arch Development Corporation. The patent was issued on application Serial No. 07/784,222, filed October 21, 1991. Because the instant application claims priority from application Serial No. 07/537,305, filed June 12, 1990, the present Applicants should be designated Senior Party, and Westbrook should be designated Junior Party.

(2) Presentation of a proposed Count

Applicants propose a Count as follows:

> A composition comprising at least two probes, each labeled with a distinguishable label, for detecting a chromosomal aberration involving the BCR and ABL genes, said chromosomal aberration having an ABL gene side and a BCR gene side, wherein one of said probes hybridizes to the ABL gene side of said chromosomal aberration and the other of said probes hybridizes to the BCR gene side of said chromosomal aberration, wherein said probes hybridize to an aberrant chromosome wherein said probes are of sufficient length to be specifically detected in cytogenetic analysis.

The proposed Count is also presented in Appendix A.

Applicants note, pursuant to 37 CFR 1.606, that the proposed Count is identical to claim 1 of the '126 patent, and to claim 127 of the present application.

(3) Identification of claims in the '126 patent corresponding to the proposed Count

According to 37 CFR 1.606, "[a]ll claims in the application and patent which define the same patentable invention as a count shall be designated to correspond to the count." "Same patentable invention" is defined by 37 CFR 1.601(n), which states

> (n) Invention "A" is the *same patentable invention* as invention "B" when invention "A" is the same as (35 U.S.C. 102) or is obvious (35 U.S.C. 103) in view of invention "B" assuming invention "B" is prior art with respect to invention "A". Invention "A" is a *separate patentable invention* with respect to invention "B" when invention "A" is new (35 U.S.C. 102) and non-obvious (35 U.S.C. 103) in view of invention "B" assuming invention "B" is prior art with respect to invention "A".

Claims 1-25, which are all of the claims of the '126 patent, correspond to the proposed Count.

Claim 1

The proposed Count is identical to claim 1 of the '126 patent.

Claim 2

Claim 2 is worded slightly differently from claim 1. A side-by-side comparison of claims 1 and 2 is shown below.

1. A composition comprising at least two probes, each labeled with a distinguishable label, for detecting a chromosomal aberration involving the BCR and ABL genes,	2. A composition comprising at least two probes for detecting a chromosomal aberration, each labeled with a distinguishable label,
said chromosomal aberration having an ABL gene side and a BCR gene side, wherein one of said probes hybridizes to the ABL gene side of said chromosomal aberration and the other of said probes hybridizes to the BCR gene side of said chromosomal aberration,	wherein one of said probes hybridizes to a part of the ABL gene on one side of said chromosomal aberration and the other of said probes hybridizes to a part of the BCR gene on the other side of said chromosomal aberration,
wherein said probes hybridize to an aberrant chromosome	wherein said probes hybridize to an aberrant chromosome
wherein said probes are of sufficient length to be specifically detected in cytogenetic analysis.	wherein said probes are of sufficient length to be specifically detected in cytogenetic analysis.

Applicants submit that Westbrook claim 2 is substantially identical in scope to claim 1. Claim 2 is thus directed to the same patentable invention as claim 1 and the Count, and so corresponds to the proposed Count.

Claim 3

Claim 3 is dependent from claim 2, which corresponds to the proposed Count. Claim 3 further limits claim 2 to probes that hybridize within 800 kb of each other in the aberrant chromosome. Westbrook asserts that this limitation is necessary so that labeled flanking

regions of a chromosomal breakpoint are "distinguishable yet juxtaposed at interphase."[3] Westbrook concedes that the use of fluorescent- labeled probes in *in situ* hybridization to interphase chromosomes was known in the art at the filing date of the application that matured into the '126 patent.[4] Accordingly, claim 3 is obvious in view of, and corresponds to, the proposed Count.

Claim 4

Claim 4 is dependent from claim 1, which corresponds to the proposed Count. Claim 4 further limits claim 1 to fluorescently labeled probes. In the paragraph bridging columns 2 and 3 of the '126 patent, Westbrook concedes that fluorescent labeling of probes was widely known in the art at the filing date of the application that matured into the '126 patent.[5] Accordingly, claim 4 is obvious in view of, and corresponds to, the proposed Count.

Claim 5

Claim 5 is dependent from claim 4, which corresponds to the proposed Count. Claim 5 further limits claim 4 to the situation where distinguishable fluorescent labels are used. Westbrook concedes that the use of multiple distinct fluorescent labels for *in situ* hybridization was known in the art at the filing date of the application that matured into the '126 patent.[6]

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[3] '126 patent, col. 6, lines 7-9 ("To be distinguishable yet juxtaposed at interphase, labeled flanking regions have to be approximately within 800 kb.").

[4] '126 patent, col. 3, lines 39-43. ("Pinkel et al. (1986, 1988) and Gray et al. (1990) relate fluorescent-labeled probes for the cytogenetic analysis of chromosomes, and in situ hybridization of chromosomes at metaphase and interphase with whole chromosome-specific DNA.")

[5] '126 patent, col. 2, line 60 - col. 3, line 3: ("As an alternative to cytogenetic analysis recently, newer methods of chromosomal *in situ* hybridization with non-isotopically labeled genetic probes have improved and extended the capabilities of cytogenetics. One of these methods is fluorescence *in situ* hybridization (FISH). In this method, probes are labeled with fluorescent signals that are detectable, generally by microscopic viewing of colors.")

[6] *Id.*

Accordingly, claim 5 is obvious in view of, and corresponds to, the proposed Count.

Claim 6

Claim 6 is dependent from claim 1, which is identical to the proposed Count. Claim 6 further limits claim 1 to the situation where the claimed probes "hybridize with chromosomal DNA *in situ* in cells." As noted above, Westbrook concedes that the use of fluorescent- labeled probes in *in situ* hybridization to interphase chromosomes was known in the art at the filing date of the application that matured into the '126 patent.[7] In view of this admission, it is clear that Claim 6 is obvious over claim 1. Claim 6 is thus directed to the same patentable invention as claim 1 and the Count, and so corresponds to the proposed Count.

Claim 7

Claim 7 is dependent from claim 6, which corresponds to the proposed Count. Claim 7 further limits claim 6 to the situation wherein *in situ* hybridization takes place during interphase. Westbrook concedes that *in situ* hybridization of chromosomes at interphase was known in the art at the filing date of the application that matured into the '126 patent.[8] In view of this admission, it is clear that claim 7 is obvious over claim 6 (and, by extension, over claim 1). Claim 7 is thus directed to the same patentable invention as claims 6 and 1, and the Count, and so corresponds to the proposed Count.

Claim 8

Claim 8 is dependent from claim 7, which corresponds to the proposed Count. Claim 8

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[7] '126 patent, col. 3, lines 39-43. ("Pinkel et al. (1986, 1988) and Gray et al. (1990) relate fluorescent-labeled probes for the cytogenetic analysis of chromosomes, and in situ hybridization of chromosomes at metaphase and interphase with whole chromosome-specific DNA.")

[8] *Id.*

further limits claim 7 to the situation wherein "the probes after hybridization are juxtaposed as doublets if a chromosomal aberration is present." "Doublets" are defined by Westbrook as "pairs of distinct probes in closer proximity than expected based on there [*sic,* their] normal chromosome locations in the absence of aberrations."[9] The appearance of doublets in cells where a translocation has occurred is inherent from the limitations of claims 1, 6, and 7, from which claim 8 depends. Accordingly, Claim 8 is obvious over claims 1, 6, and 7. Claim 8 is thus directed to the same patentable invention as claims 7, 6, and 1, and the Count, and so corresponds to the proposed Count.

Claim 9

Claim 9 is dependent from claim 1, which corresponds to the proposed Count. Claim 9 further limits claim 1 to an embodiment where one probe "is capable of hybridizing to a least a portion of the last exon of the ABL gene" while a second probe "is capable of hybridizing to at least a portion of exon I of the BCR gene." Westbrook concedes that the structure of the BCR gene and its first exon, of the ABL gene and its last exon, and their relationship to CML and ALL, were known in the art at the filing date of the application that matured into the '126 patent. Accordingly, it would have been obvious to construct a probe to that region in order to diagnose CML or ALL. Consequently, claim 9 is obvious in view of, and corresponds to, the proposed Count.

Claim 10

Claim 10 depends from claim 8, and further limits claim 8 to the situation wherein the chromosomal aberration comprises a translocation formed by breakpoints which occur on the long arms of human chromosomes 9 and 22. Westbrook concedes that the location of the

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[9] '126 patent, col 5, lines 64-66.

breakpoints associated with CML, on the long arms of chromosomes 9 and 22 , was known in the art at the filing date of the application that matured into the '126 patent.[10] In view of this admission, it is clear that Claim 10 is obvious over claim 8 (and, by extension, over claim 1). Claim 10 is thus directed to the same patentable invention as claims 8 and 1, and the Count, and so corresponds to the proposed Count.

Claim 11

Claim 11 depends from claim 10, and further limits claim 10 to the situation where the translocation breakpoints occur at "locations designated t(9:22)(q11;q34)." Westbrook concedes that the location of the breakpoints associated with CML, at locations designated t(9;22)(q11;q34), was published by Rowley in 1973.[11] In view of this admission, it is clear that Claim 11 is obvious over claim 10 (and, by extension, over claim 1). Claim 11 is thus directed to the same patentable invention as claims 10 and 1, and the Count, and so corresponds to the proposed Count.

Claim 12

Claim 12 depends from claim 11, and further limits claim 11 to the situation where "the translocation breakpoints are further defined to occur in the BCR and ABL genes" and wherein "a fusion gene is formed by the translocation, and said fusion gene comprises portions of the BCR and ABL genes." Westbrook concedes that it was known in the art, prior to the filing of the application that matured into the '126 patent, that translocations between the BCR and ABL genes resulted in fusion genes comprising portions of the BCR and ABL genes.[12] In view of this

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[10] *See, e.g.*, '126 patent, col. 11, lines 33 – 36 ("The molecular basis of the Ph' chromosome is a translocation between the long arms of chromosomes 9 and 22, t(9;22)(q11;q34)(Rowley, 1973)."

[11] *Id.*

[12] *See, e.g.*, '126 Patent, col. 11, lines 33-53.

admission, it is clear that Claim 11 is obvious over claim 10 (and, by extension, over claim 1). Claim 11 is thus directed to the same patentable invention as claims 10 and 1, and the Count, and so corresponds to the proposed Count.

Claim 13

Claim 13 is dependent from claim 12, and further limits claim 12 to a fusion gene encoding p190. The only fusion gene disclosed by Westbrook to encode p190 is the Philadelphia chromosome. The Philadelphia chromosome is conceded by Westbrook to have been known in the art at the filing date of the application that matured into the '126 patent.[13] Accordingly, claim 13 is obvious in view of, and corresponds to, claim 12 and the proposed Count.

Claim 14

Claim 14 is dependent from claim 6, which corresponds to the proposed Count. Claim 14 further limits claim 6 to a composition for use on DNA *in situ* in human cells. Westbrook concedes that *in situ* hybridization to DNA in human cells was known in the art at the filing date of the application that matured into the '126 patent. Accordingly, claim 14 is obvious in view of, and corresponds to, the proposed Count.

Claim 15

Claim 15 is dependent from claim 14, which corresponds to the proposed Count. Claim 15 further limits claim 14 to human peripheral blood cells. The practice of *in situ* hybridization on human peripheral blood cells was known in the art at the filing date of the application that matured into the '126 patent. Accordingly, claim 15 is obvious in view of, and corresponds to,

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[13] '126 patent, col. 2, lines 1-19.

the proposed Count.

Claim 16

Claim 16 is dependent from claim 15, which corresponds to the proposed Count. Claim 16 further limits claim 15 to human bone marrow cells. As claim 15 is already limited to peripheral blood cells, claim 16 appears to be *per se* indefinite. It is likely that this is due to a typographical error, and that claim 16 should properly depend from claim 14. In either case, the practice of *in situ* hybridization on human bone marrow cells was known in the art at the filing date of the application that matured into the '126 patent. Accordingly, claim 16 is obvious in view of claims 14 and 15, and corresponds to the proposed Count.

Claim 17

Claim 17 is dependent from claim 6, which corresponds to the proposed Count. Claim 17 further limits claim 6 to cultured cells. The use of cultured cells was known in the art at the filing date of the application that matured into the '126 patent.[14] Accordingly, claim 17 is obvious in view of claim 6, and corresponds to the proposed Count.

Claim 18

Claim 18 is dependent from claim 1, which is identical to the proposed Count. Claim 18 further limits claim 1 to a composition where one of the probes "is capable of hybridizing to the major breakpoint cluster region (M-bcr) of chromosome 22." Westbrook concedes that the structure of the M-bcr region of chromosome 22, and its relationship to CML and ALL, were

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[14] '126 patent, col 3, line 64 - col. 4, line 3 ("Flow cytometry has been applied to detection and characterization of disease-linked chromosomal aberrations (Gray et al. 1990). There is a great need to improve methods of detecting specific chromosome aberrations. Flow cytometric requires in vitro cell culture, expensive equipment, and expertise in interpretation of statistical analyses of results. Therefore, it is not generally clinically useful.")

known in the art at the filing date of the application that matured into the '126 patent. Accordingly, it would have been obvious to construct a probe to that region in order to diagnose CML or ALL. Consequently, claim 18 is obvious in view of claim 1, and corresponds to the proposed Count.

Claim 19

Claim 19 is dependent from claim 1, which is identical to the proposed Count. Claim 19 further limits claim 1 to a composition where one of the probes "is capable of hybridizing to the first exon of the BCR gene." Westbrook concedes that the structure of the BCR gene and its first exon, and their relationship to CML and ALL, were known in the art at the filing date of the application that matured into the '126 patent. Accordingly, it would have been obvious to construct a probe to that region in order to diagnose CML or ALL. Consequently, claim 19 is obvious in view of claim 1, and corresponds to the proposed Count.

Claim 20

Claim 20 is dependent from claim 1, which is identical to the proposed Count. Claim 20 further limits claim 1 to the embodiment where one probe "is capable of hybridizing at least a part of the last exon of the ABL gene." Westbrook concedes that the structure of the ABL gene and its last exon, and their relationship to CML and ALL, were known in the art at the filing date of the application that matured into the '126 patent. Moreover, Westbrook states that "the last exon of the ABL gene . . . is a necessary part of the BCR-ABL fusion gene."[15] Accordingly, it would have been obvious to construct a probe to that region in order to diagnose CML or ALL. Accordingly, claim 20 is obvious in view of, and corresponds to, claim 1 and the proposed Count.

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[15] '126 patent, col. 11, lines 56-58.

Claim 21

Claim 21 is dependent from claim 12, which corresponds to the proposed Count. Claim 21 further limits claim 12 to compositions wherein the probes bind to a fusion gene that encodes either of two proteins: p190 or p210. The only fusion gene disclosed by Westbrook to be diagnostic or prognostic for ALL is the Philadelphia chromosome. The Philadelphia chromosome is conceded by Westbrook to have been known in the art at the filing date of the application that matured into the '126 patent.[16] Westbrook concedes that both p190 and p210, and their importance in CML and ALL, were known in the art at the filing date of the application that matured into the '126 patent.[17] Consequently it would have been obvious, at the time the Westbrook application was filed, to construct probes to detect the fusion gene encoding p190 or p210 in order to detect CML or ALL. Claim 21 is thus obvious in view of, and thus corresponds to, claim 12 and the proposed Count.

Claim 22

Claim 22 is dependent from claim 21, which corresponds to the proposed Count. Claim 22 further limits claim 21 to situations where the fusion gene is diagnostic or prognostic for acute lymphocytic leukemia (ALL). The only fusion gene disclosed by Westbrook to be diagnostic or prognostic for ALL is the Philadelphia chromosome. The Philadelphia chromosome is conceded by Westbrook to have been known in the art at the filing date of the

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[16] '126 patent, col. 2, lines 1-19.

[17] *See* '126 patent, col. 11, lines 44-53 ("Two types of BCR-ABL fusion genes exist in ALL. One type has a BCR breakpoint in the limited region of the M-bcr (Groffen et al. 1984) and produces a 210 kd protein, designated p210. This is the type of fusion gene found in virtually all cases of CML. The other type of fusion gene has a BCR breakpoint in the large region of the BCR first intron (Rubin et al., 1988: Heisterkamp et al., 1988) and it produces a 190 kD protein, p. 190. This type of fusion gene accounts for 75% of the Ph^1 positive cases of ALL, the remainder having the p210 arrangement.").

application that matured into the '126 patent.[18] Accordingly, claim 22 is obvious in view of claim 21, and corresponds to, the proposed Count.

Claim 23

Claim 23 is dependent from claim 21, which corresponds to the proposed Count. Claim 23 further limits claim 21 to situations where the fusion gene is diagnostic or prognostic for chronic myelogenous leukemia (CML). The only fusion gene disclosed by Westbrook to be diagnostic or prognostic for CML is the Philadelphia chromosome. The Philadelphia chromosome is conceded by Westbrook to have been known in the art at the filing date of the application that matured into the '126 patent.[19] Accordingly, claim 22 is obvious in view of claim 23, and corresponds to the proposed Count.

Claim 24

Claim 24 is an independent kit claim that substantially duplicates claim 1, which is identical to the proposed Count. The only notable difference between the claims is that claim 24 recites a kit comprising "a first and second nucleic acid probe" (*i.e.*, two probes) while claim 1 recites a composition comprising "at least two probes." A composition comprising two probes is indisputably an obvious species of a composition comprising "at least two" probes. Moreover, packaging of reagents in kit form is and was conventional in the art. Accordingly, claim 24 is obvious in view of, and corresponds to, the proposed Count.

Claim 25

Claim 25 is dependent from claim 1, which corresponds to the proposed Count. Claim

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[18] '126 patent, col. 2, lines 1-19.

[19] *Id.*

25 further limits claim 1 to a composition for detecting aberrations in the Philadelphia chromosome. The Philadelphia chromosome is conceded by Westbrook to have been known in the art at the filing date of the application that matured into the '126 patent.[20] Accordingly, claim 25 is obvious in view of claim 1, and corresponds to the proposed Count.

(4) Presentation of claims corresponding to the proposed Count and explanation why such claims correspond to the proposed Count.

Claims 127-128, 130-134, 136-142, and 146-149 of the present application correspond to the proposed Count. It will be readily appreciated that Claim 127 and the proposed Count are identical and therefore, claim 127 corresponds to the proposed Count. As claims 128, 130-134, 136-142, and 146-149 are substantially identical to Westbrook claims 2, 4-8, 10-12, 14-17, and 22-25, Applicants submit that claims 128, 130-134, 136-142, and 146-149 of the instant application correspond to the proposed Count for the reasons set forth in the discussion of the Westbrook claims above.

(5) Applying terms of application claims to the disclosure of the application

Attached hereto as Appendix B is a chart providing an element-by-element recitation of the claims of the present application and an indication of exemplary passages in the application where, at the very least, the claims find full support. Applicants emphasize that this support set forth in this chart is only exemplary, and reserve the right to supplement the support for each claim as necessary or desired.

(6) The Requirements of 35 USC 135(b)(1) Are Satisfied.

Section (b)(1) of 35 USC 135 requires that

> A claim which is the same as, or for the same or substantially the same subject matter as, a claim of an issued patent may not be made in any application unless

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[20] *Id.*

such a claim is made prior to one year from the date on which the patent was granted.

The pending claims in the present application were added by Applicants' Preliminary Amendment filed February 15, 2001. As this is one year after the issuance of the '126 patent on February 15, 2000, the terms of 35 USC 135(b)(1) are satisfied.

(7) Conclusion

Applicants respectfully request that examination of the present application be expedited. Applicants also request that an interference be declared:

(i) employing the proposed Count set forth in attached Appendix A;

(ii) with claims 1-25 of the '126 patent and claims 127-128, 130-134, 136-142, and 146-149 of the present application designated as corresponding to the proposed Count; and

(iii) Applicants indicated to be entitled to the benefit of the applications listed in footnote 2, above.

Further, upon a determination by the Examiner that an interference should be declared, issuance of a Notice suspending prosecution pending declaration of an interference is respectfully requested. The above actions are respectfully requested.

Respectfully submitted,

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